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L4: Entry 16 of 17

May 22, 2001

DOCUMENT-IDENTIFIER: US 6235481 B1

TITLE: Polynucleotides encoding calpain 10

Drawing Description Text (11):

FIG. 9A, FIG. 9B and FIG. 9C. Effect of protease inhibitors on the insulin secretory response to glucose and other secretagogues in mouse pancreatic islets. FIG. 9A Insulin secretion by islets incubated at various glucose concentrations in the absence (open bars) and presence (hatched bars) of 100 .mu.M ALLM. Results are mean .+-.SEM of 4-7 studies per group. *p<0.05 compared to islets incubated in the absence of ALLM. FIG. 9B. Insulin secretion by perifused islets in response to stimulation with 20 $\ensuremath{\text{mM}}$ glucose (6-20min, solid bar). The perifusate contained 2 mM glucose except where shown. Islets were preincubated for 4 hr either in the absence of calpain inhibitors (.box-solid.) or in the presence of 100 .mu.M ALLM (.circle-solid.) or 200 .mu.M E-64-d (.tangle-solidup.). In studies involving inhibitors, ALLM was present throughout the study but E-64-d which is an irreversible cysteine protease inhibitor was present only during the pre-incubation. Results are mean .+-.SEM of 3 studies in each group. FIG. 9C. Insulin secretion by mouse islets incubated in the presence of 2 mM glucose (2), 8 mM glucose (8), 250 .mu.M carbachol (CCh) or 50 nM $\underline{\text{GLP-1}}$ in the presence of 8 mM glucose and 30 mM KCl in the presence of 2 mM glucose (KCl). Islets were incubated either in the absence (open bars) or presence (hatched bars) of 100 .mu.M ALLM. Results are mean .+-.SEM of 6 separate studies. *p<0.05 compared to islets incubated in the absence of ALLM.

Detailed Description Text (25):

Some patients are virtually impossible to treat with insulin because their cells cannot effectively utilize or are resistant to insulin therapy. As a result of the lack of glycemic control, diabetic patients often experience a variety of conditions including: neuropathy, nephropathy, cardiomyopathy, fetinopathy, coronary and peripherovascular disease and the like. These complications occur due to the unachieved glycemic control that results from failure of the insulin, diet and/or exercise only approach.

Detailed Description Text (473):

Animals. Studies were performed on islets obtained from non-fasted 9-13 wk old C57BL/6J mice (Jackson, Bar Harbor, Me.) and adipocytes and soleus muscles isolated from 8-12 wk old normal Wistar rats (Harlan Sprague-Dawley, Indianapolis, Ind.). The calpain inhibitors used were ALLM (N-Ac-Leu-Leu-methioninal, Calbiochem-Novabiochem, Inc, San Diego, Calif.) and E-64-d (ethyl

(+)-(2S,3S)-3-[(S)-3-Methyl-1-(3-methylbutylcarbamoyl)butyl-carbamoyl]-2-o xiranecarboxylate, Matreya Inc., Pleasant Gap, Pa.). The calpain inhibitors were dissolved in DMSO. GLP-1 (7-36 amide) was from Peninsula Laboratory (Belmont, Calif.).

Detailed Description Text (490):

ALLM (250 .mu.M) and E-64-d (200 .mu.M) increased the insulin secretory responses to 20 mM glucose in isolated pancreatic islets by 1.97.+-.0.3-fold (n=5, p<0.01, (mean.+-.SEM)) and 1.77.+-.0.1-fold (n=6, p<0.001), respectively (FIG. 8A and FIG. 8B). These effects were not observed at 2 mM glucose. The effects of ALLM and E-64-d on the insulin secretory response to 20 mM glucose (FIG. 8C and FIG. 8D) were seen at inhibitor concentrations greater than 100 .mu.M and were glucose dependent in that the insulin secretory response was enhanced at glucose concentrations above 8 mM glucose but significant effects were not observed at 2,4 or 6 mM glucose (FIG. 9A). The

enhancement of the insulin secretory response to 20 mM glucose by ALLM and E-64-d was also observed in a dynamic islet perifusion system (FIG. 9B). ALLM produced a small but statistically significant increase in the insulin secretory response to 50 nM $\underline{\text{GLP-1}}$ (1.55.+-.0.2-fold, n=6, p<0.05), an agent which stimulates adenyl cyclase. ALLM did not however significantly increase the insulin secretory responses to 30 mM KCl, an agent which directly depolarizes the .beta.-cell (FIG. 9C) or 100 .mu.M carbachol (CCh) which mobilizes Ca.sup.2+ from intracellular stores.

Detailed Description Text (500):

The present studies also provide insight into the molecular mechanism by which ALLM and E-64-d increase the insulin secretory responses to glucose and GLP-1. These agents did not lead to an increase in [Ca.sup.2+].sub.i, rates of glucose oxidation and utilization, or NAD(P)H generation. Thus, they do not affect pathways in the .beta.-cell responsible for the uptake and metabolism of glucose. Rather, the inventors believe that the most likely site(s) of action are in pathways that regulate the movement or fusion of insulin secretory granules with the plasma membrane.

Generate Collection Print

L4: Entry 14 of 17

File: USPT

Jun 4, 2002

DOCUMENT-IDENTIFIER: US 6399601 B1

TITLE: Bicyclic pyrrolyl amides as glycogen phosphorylase inhibitors

Brief Summary Text (156):

GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)-NH.sub.2;

Brief Summary Text (175):

In another preferred embodiment of the kits, the second compound is selected from LysPro insulin, GLP-1 (7-37) (insulinotropin), GLP-1 (7-36)-NH.sub.2, chlorpropamide, glibenclamide, tolbutamide, tolazamide, acetohexamide, glypizide, glimepiride, repaglinide, meglitinide; metformin, phenformin, buformin, midaglizole, isaglidole, deriglidole, idazoxan, efaroxan, fluparoxan, linogliride, ciglitazone, pioglitazone, englitazone, troglitazone, darglitazone, rosiglitazone, clomoxir, etomoxir. acarbose, miglitol, emiglitate, voglibose, MDL-25,637, camiglibose, MDL-73,945, BRL 35135, BRL 37344, Ro 16-8714, ICI D7114, CL 316,243, L-386,398; benfluorex, fenfluramine, Naglivan.RTM., (bis(cysteinamide N-octyl)oxovanadium) acpimox, WAG 994, Symlin.TM., (pramlintide acetate)-AC2993 and nateglinide.

Brief Summary Text (265):

Representative agents that can be used to treat diabetes include insulin and insulin analogs: (e.g., LysPro insulin. inhaled formulations comprising insulin); GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)NH.sub.2; sulfonylureas and analogs: chlorpropamide, glibenclamide, tolbutamide, tolazamide, acetohexamide, glypizide, glimepiride, repaglinide, meglitinide; biguanides: metformin, phenformin, buformin; .alpha.2-antagonists and imidazolines: midaglizole, isaglidole, deriglidole, idazoxan, efaroxan, fluparoxan; other insulin secretagogues: linogliride, insulinotropin, exendin-4, BTS-67582, A-4166; glitazones: ciglitazone, pioglitazone, englitazone, troglitazone, darglitazone, rosiglitazone; PPAR-gamma agonists; RXR agonists: JTT-501, MCC-555, MX-6054, DRF2593, GI-262570, KRP-297, LG100268; fatty acid oxidaton inhibitors: clomoxir, etomoxir; .alpha.-glurosidase inhibitors: precose, acarbose, miglitol, emiglitate, voglibose, MDL-25,637, camiglibose, MDL-73,945; .beta.-agonists: BRL 35135, BRL 37344, Ro 16-8714, ICI D7114, CL 316,243, TAK-667, AZ40140; phosphodiesterase inhibitors, both cAMP and cGMP type: sildenafil, L686398: L-386,398; lipid-lowering agents: benfluorex, atorvastatin; antiobesity agents: fenfluramine, orlistat, sibutramine; vanadate and vanadium complexes (e.g., Naglivan.RTM.) and peroxovanadium complexes; amylin antagonists: pramlintide, AC-137; lipoxygenase inhibitors: masoprocal; somatostatin analogs: BM-23014, seglitide, octreotide; glucagon antagonists: BAY 276-9955; insulin signaling agonists, insulin mimetics, PTP1B inhibitors: L-783281, TER17411, TER17529; gluconeogenesis inhibitors:GP3034; somatostatin analogs and antagonists; antilipolytic agents: nicotinic acid, acipimox, WAG 994; glucose transport stimulating agents: BM-130795; glucose synthase kinase inhibitors: lithium chloride, CT98014, CT98023; galanin receptor agonisnts; MTP inhibitors such as those disclosed in U.S. provisional patent application No. 60/164,803; growth hormone secretagogues such as those disclosed in PCT publication numbers WO 97/24369 and WO 98/58947; NPY antagonists: PD-160170, BW-383, BW1229, CGP-71683A, NGD 95-1, L-152804; Anorectic agents including 5-HT and 5-HT2C receptor antagonists and/or mimetics: dexfenfluramine, Prozac.RTM., Zoloft.RTM.; CCK receptor agonists: SR-27897B; galanin receptor antagonists; MCR-4 antagonists: HP-228; leptin or mimetics:leptin; 11-beta-hydroxysteroid dehydrogenase type-I inhibitors; urocortin mimetics, CRF antagonists, and CRF binding proteins: RU486, urocortin. Other anti-diabetic agents that can be used in combination with a glycogen phosphorylase inhibitor include ergoset and D-chiroinositol. Any combination of agents can be

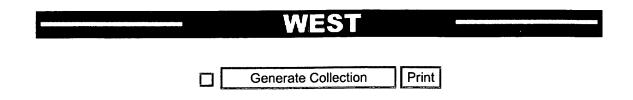
administered as described above.

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Brief Summary Text (360):
The compounds of the present invention can also be used in combination with sorbitol
dehydrogenase inhibitors. Sorbitol dehydrogenase inhibitors lower fructose levels and
have been used to treat or prevent diabetic complications such as neuropathy,
retinopathy, nephropathy, cardiomyopathy, microangiopathy, and macroangiopathy. U.S.
Pat. Nos. 5,728,704 and 5,866,578 disclose compounds and a method for treating or
preventing diabetic complications by inhibiting the enzyme sorbitof dehydrogenase.
CLAIMS:
13. The pharmaceutical composition of claim 12 wherein the second compound is useful
to treat diabetes and is selected from:
insulin and insulin analogs;
GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)--NH.sub.2;
sulfonylureas and analogs;
biguanides;
.alpha.2-antagonists;
imidazolines;
glitazones (thiazolidinediones);
PPAR-gamma agonists
fatty acid oxidation inhibitors;
.alpha.-glucosidase inhibitors;
.beta.-agonists;
phosphodiesterase Inhibitors;
lipid-lowering agents:
antiobesity agents
vanadate, vanadium complexes and peroxovanadium complexes;
amylin antagonists;
glucagon antagonists;
gluconeogenesis inhibitors;
somatostatin analogs and antagonists; or
antilipolytic agents.
14. The pharmaceutical composition of claim 12 wherein the second compound is useful
to treat diabetes and is selected from:
LysPro insulin, GLP-1 (7-37) (insulinotropin), GLP-1 (7-36)--NH.sub.2, chlorpropamide,
glibenclamide, tolbutamide, tolazamide, acetohexamide, glypizide, glimepiride,
repaglinide, meglitinide; mefformin, phenformin, buformin, midaglizole, isaglidole,
deriglidole, idazoxan, efaroxan, fluparoxan, linogliride, ciglitazone, pioglitazone,
englitazone, troglitazone, darglitazone, rosiglitazone, clomoxir, etomoxir, acarbose,
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miglitol, emiglitate, voglibose, MDL-25,637, camiglibose, MDL-73,945, BRL 35135, BRL

37344, Ro 16-8714, ICI D7114, CL 316,243, L-386,398; benfluorex, fenfluramine,

(bis(cysteinamide N-octyl)oxovanadium), acipimox, WAG 994, Symlin.TM., (pramlintide acetate) AC2993 or nateglinide.



L4: Entry 13 of 17

File: USPT

Aug 27, 2002

DOCUMENT-IDENTIFIER: US 6441015 B2

TITLE: Tetrazole compounds as thyroid receptor ligands

Brief Summary Text (97):

Representative agents that can be used to treat diabetes in combination with a compound of the present invention include insulin and insulin analogs (e.g. LysPro insulin); $\underline{GLP-1}$ (7-37) (insulinotropin) and $\underline{GLP-1}$ (7-36)--NH.sub.2; sulfonylureas and analogs: chlorpropamide, glibenclamide, tolbutamide, tolazamide, acetohexamide, glypizide, glimepiride, repaglinide, meglitinide; biguanides: metformin, phenformin, buformin; .alpha.2-antagonists and imidazolines: midaglizole, isaglidole, deriglidole, idazoxan, efaroxan, fluparoxan; other insulin secretagogues: linogliride, A-4166; glitazones: ciglitazone, pioglitazone, englitazone, troglitazone, darglitazone, BRL49653; fatty acid oxidation inhibitors: clomoxir, etomoxir; .alpha.-glucosidase inhibitors: acarbose, miglitol, emiglitate, voglibose, MDL-25,637, camiglibose, MDL-73,945; .beta.-agonists: BRL 35135, BRL 37344, RO 16-8714, ICI D7114, CL 316,243; phosphodiesterase inhibitors: L-386,398; lipid-lowering agents: benfluorex; antiobesity agents: fenfluramine; vanadate and vanadium complexes (e.g. Naglivan.RTM.) and peroxovanadium complexes; amylin antagonists; glucagon antagonists; gluconeogenesis inhibitors; somatostatin analogs; antilipolytic agents: nicotinic acid, acipimox, WAG 994. Also contemplated to be used in combination with a compound of the present invention are pramlintide (symlin.TM.), AC 2993 and nateglinide. Any agent or combination of agents can be administered as described above.

Brief Summary Text (115):

The compounds of the present invention can also be used in combination with a sorbitol dehydrogenase inhibitor. Sorbitol dehydrogenase inhibitors lower fructose levels and have been used to treat or prevent diabetic complications such as neuropathy, retinopathy, nephropathy, cardiomyopathy, microangiopathy, and macroangiopathy. U.S. Pat. Nos. 5,728,704 and 5,866,578 disclose compounds and a method for treating or preventing diabetic complications by inhibiting the enzyme sorbitol dehydrogenase.

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NEWS 11
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NEWS 18 Aug 08
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NEWS 19 Aug 19
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         Sep 16 Experimental properties added to the REGISTRY file
NEWS 25
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NEWS 26
         Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27
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NEWS 28 Oct 21 EVENTLINE has been reloaded
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     function due to localized reduced perfusion. Hibernating myocytes retain
     cellular integrity, but cannot sustain high-energy requirements of
     contraction. High plasma levels of catecholamines, such as
     norepinephrine, are believed to be predictive of mortality from
    hibernating myocardium. Likewise, high levels of catecholamines lead to
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     reduces plasma norepinephrine levels, and it thus is useful in a method of
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    Treatment of hibernating myocardium and diabetic cardiomyopathy
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T.4
     Hibernating myocardium is characterized by viable myocardium with impaired
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     function due to localized reduced perfusion. Hibernating myocytes retain
     cellular integrity, but cannot sustain high-energy requirements of
     contraction. High plasma levels of catecholamines, such as
     norepinephrine, are believed to be predictive of mortality from
     hibernating myocardium. Likewise, high levels of catecholamines lead to
     cardiomyopathy in patients with diabetes. GLP-1
     reduces plasma norepinephrine levels, and it thus is useful in a method of
     treating hibernating myocardium or diabetic cardiomyopathy.
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     Treatment of hibernating myocardium and diabetic cardiomyopathy
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L9: Entry 2 of 2

File: USPT

Dec 11, 2001

DOCUMENT-IDENTIFIER: US 6329389 B1

TITLE: Amine compounds, their production and use

Brief Summary Text (561):

The "hormones" include, for example, growth hormone (GH), growth hormone-releasing hormones (GHRH), thyroid stimulating hormone(TSH), prolactin, insulin, glucagon, etc. The "growth factors" include, for example, insulin-like growth factor-i (IGF-1) and vascular endothelial cell growth factor (VEGF). The "physiologically active substances" include, for example, vasoactive intestinal polypeptide (VIP), gastrin, glucagon-like peptide-1, amylin, substance-P, CCK(cholecystokinin), amylase, interleukins such as interleukin-1 (IL-1) and etc., cytokines such as TNF-.alpha. and etc., cardiotropin, etc.

Brief Summary Text (563):

Compounds (I) and (I') are useful (1) for drugs for treatment of tumors such as acromegaly, TSH-producing tumors, nonsecretory (afunctional) hypophysial tumors, ectopic ACTH (adrenocorticotrophic hormone)-producing tumors, medullar thyroid carcinoma, VIP-producing tumors, glucagon-producing tumors, gastrin-producing tumors, insulinoma and carotinoid tumor, (2) for drugs for treatment of insulin-dependent and non-insulin dependent diabetes mellitus or a variety of diseases associated with them, namely diabetic complications such as diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, Doan syndrome and orthostatic hypotension, (3) for drugs for improvement of hyperinsulinemia or for treatment of obesity caused by inhibition of appetite, and overeating, (4) for drugs for treatment of acute pancreatitis, chronic pancreatitis, pancreal/intestinal fistula, hemorrhagic ulcer, peptic ulcer, gastritis, hyperchylia, regurgitant esophagitis, (5) for drugs for improvement of various symptoms associated with the Helicobacter pylori infection, for example, inhibitors of gastrin hypersecretion, (6) for drugs for inhibition of amylase secretion associated with endoscopic cholangiopancreatography, and drugs for prognostic treatment of surgical operation of pancreas, (7) for drugs for treatment of diarrhea due to intestinal malabsorption, promotion of secretion or dyskinesia of the digestive tracts (for example, short bowel syndrome), diarrhea due to the drugs for cancer chemotherapy, diarrhea due to congenital small intestine atrophy, diarrhea due to neuroendocrine tumors such as VIP-producing tumors, diarrhea due to AIDS, diarrhea due to graft versus host reaction associated with bone marrow transplantation, diarrhea due to diabetes mellitus, diarrhea due to celiac plexus blocking, diarrhea due to systemic sclerosis and diarrhea due to eosinophilia, (8) for drugs for treatment of dumping syndrome, irritable colitis, Crohn disease and inflammatory bowel disease, (9) for drugs for treatment of tumors or cancers (e.g., thyroid cancer, large bowel cancer, breast cancer, prostatic cancer, small cell lung cancer, non-small cell cancer, pancreatic cancer, stomach cancer, cholangiocarcinoma, hepatic cancer, vesical cancer, ovarian cancer, melanoma, osteosarcoma, chondrosarcoma, malignant pheochromocytoma, neuro-blastoma, brain tumors, thymoma, renal cancers), leukemia (e.g., leukemia of basophilic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, Hodgkin disease, and non-Hodgkin lymphoma) (drugs for treatment of these cancers can be used for monotherapy or concomitant therapy with other anticancer drugs such as Tamoxifen, LHRH agonists, LHRH antagonists, interferon-.alpha., .beta. and .gamma., interleukin-2 and etc,), (10) for drugs for prevention and treatment of hypertrophic cardiomyopathy, arteriosclerosis, valvular disease, myocardiac infarction (especially, myocardiac infarction post percutaneous transluminal coronary arterioplasty) and reangioplasty, (11) for drugs for treatment of hemorrhage of

esophageal varicosis, cirrhosis and peripheral blood vessel disorders, (12) for drugs for treatment of diseases associated with general or local inflammation, for example, polyarteritis, rheumatoid arthritis, psoriasis, sunburn, eczema and allergy (e.g., asthma, atopic dermatitis and allergic rhinitis) because they inhibit or modulate the secretion of physiologically active substances acting on the immune system (e.g., Substance P, tachykinin and cytokines), (13) for drugs for treatment of dementia (e.g., Alzheimer disease, Alzheimer-type senile dementia, vascular/multi-infarct dementia), schizophrenia, epilepsy, depression, generalized anxiety disorder, sleep disorder, and multiple sclerosis, because they give influence on the production and secretion of nerve regulators, (14) for drugs for treatment of oculopathy (e.g., glaucoma, etc.), (15) for drugs for prevention and treatment of acute bacterial meningitis, acute virus encephalitis, adult respiratory distress syndrome, bacterial pneumonia, severe systemic mycotic infection, tuberculosis, spinal damage, bone fracture, hepatic failure, pneumonia, alcoholic hepatitis, virus A hepatitis, virus B hepatitis, virus C hepatitis, AIDS infection, human papilloma virus infection, influenza infection, metastasis of cancer, multiple myeloma, osteomalacia, osteoporosis, bone Paget disease, nephritis, renal failure, sepsis, septic shock, hypercalcemia, C: hypercholesterolemia, hypertriglyceridemia, hyperlipemia, systemic lupus erythematosus, transient ischemic attach and alcoholic hepatitis, (16) for cure of organ transplantation, burns, trauma, and alopecia, (17) as analgesics for chronic or acute pain (e.g., postoperative pain, inflammatory pain, dental pain, bone disease (e.g., arthritis, rheumatism, osteoporosis etc.) derived pain), (18) for imaging of tumors having somatostatin receptors after administering radioactive substance (e.g., .sup.123 I, .sup.125 I, .sup.111 In, etc.) to compound (I) or (I') either directly or via a suitable spacer, and (19) for targeting tumors with somatostatin receptors using compound (I) or (I') conjugated with anti-cancer drugs directly or using a suitable spacer.

End of Result Set

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File: USPT

L7: Entry 1 of 1

Mar 5, 2002

DOCUMENT-IDENTIFIER: US 6352982 B1

TITLE: 4,1-benzoxazepines, their analogues, and their use as somatostatin agonists

Brief Summary Text (300):

The compounds (I) of the present invention or salts thereof may be used in a wide variety of prophylactic, diagnostic, and therapeutic treatments of mammals(for example, human, cattle, horse, dog, cat, monkey, mouse and rat, especially, human) with low toxicity and with less adverse reactions. The compounds (I) of the present invention or salts thereof inhibit or modulate production or secretion of a variety of hormones, growth factors and physiologically active substances of mammals. As said "hormones" are mentioned, for example, growth hormones (GH), thyroid stimulating hormones (TSH), prolactin, insulin and glucagon. As said "growth factors" are mentioned, for example, IGF-1. As said "physiologically active substances" are mentioned, for example, vasoactive intestinal polypeptide (VIP), gastcin, glucagon-like peptide-1, amylin, substance-P, CGRP, CCK(cholecystokinin) and amylase. And that said "physiologically active substance" includes cytokines such as interleukins and TNF-.alpha.. The compounds or salts thereof of this invention function through somatostatin receptors which couple to a variety of intracellular signal transduction systems. These systems include adenylyl cyclase, K.sup.+ channels, Ca.sup.2+ channels, protein phosphatases, phospholipaseC/IP3(inositol 1,4,5-trisphosphate), MAP kinase, a Na.sup.+ /H.sup.+ exchanger, phospholipase A2, a transcription factor such as NF-.kappa.B. The compounds or salts thereof of this invention modulate directly or indirectly cell proliferation inhibitory action of somatostatin and modulate apoptosis induced or regulated by somatostatin. The compounds or salts thereof of this invention may be used in a variety of diseases associated with disorders of production or secretion of hormones, growth factors, and physiologically active substances, associated with disorders of intracellular signal transduction systems, or associated with disorders of regulating cell proliferation. Preferably, the compounds or salts thereof of this invention may be useful (1) for drugs for treatment of for example, tumors such as acromegaly, TSH-producing tumors, nonsecretory (afunctional) hypophysial tumors, ectopic ACTH (adrenocorticotrophic hormone)-producing tumors, medullar thyroid carcinoma, VIP-producing tumors, glucagon-producing tumors, gastrin-producing tumors, insulinoma and cartinoid tumor, (2) for drugs for treatment of insulin-dependent and non-insulin dependent diabetes mellitus or a variety of diseases associated with them, for example, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, Doan syndrome and orthostatic hypotension, (3) for drugs for improvement of hyperinsulinemia or for treatment of obesity, for example, by inhibition of appetite (4) for drug for treatment of, for example, acute pancreatitis, chronic pancreatitis, pancreatointestinal fisutula, hemorrhagic ulcer, peptic ulcer, gastritis and hyperchylia by inhibition or modulation of the exocrine secretion in the digestive tracts, (5) for drugs for improvement of various symptoms associated with the Helicobacter pylori infection, for example, inhibitors of gastrin hypersecretion, (6) for drugs for inhibition of amylase secretion associated with endoscopic cholangiopancreatography, and drugs for prognostic treatment of surgical operation of pancreas, (7) for drugs for treatment of, for example, diarrhea due to intestinal malabsorption, promotion of secretion or dyskinesia of the digestive tracts(for example, short bowel syndrome), diarrhea due to the drugs for cancer chemotherapy, diarrhea due to AIDS, diarrhea due to graft versus host reaction (GVHR) associated with bone marrow transplantation, diarrhea due to diabetes mellitus, diarrhea due to celiac plexus blocking, diarrhea due to systemic sclerosis and diarrhea due to eosinophilia, (8) for drugs for treatment of, for

example, dumping syndrome, irritable bowel syndrome, Crohn disease and inflammatory bowel disease, (9) for drugs for treatment of, for example, various cancers and tumors of which growth is dependent on insulin or IGF-1 or the other growth factors and various tumors and cancers associated with disorders of regulating cell proliferation caused by the other reasons (for example, thyroid cancer, colorectal cancer, breast cancer, prostatic cancer, small cell lung cancer, non-small cell cancer, pancreatic cancer, stomach cancer, cholangiocarcinoma, hepatic cancer, vesical cancer, ovarian cancer, melanoma, osteosarcoma, chondrosarcoma, malignant pheochromocytoma, neuro-blastoma, brain tumors, thymoma, renal cancers), leukemia (for example, leukemia of basophilic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, Hodgkin disease, and non-Hodgkin lymphoma) (drugs for treatment of these cancers can be used for monotherapy or concomitant therapy with other anticancer drugs, for example, tamoxifen, LHRH agonists, LHRH antagonists, interferon-.alpha., Interferon-.beta., interferon-.gamma. and interleukin-2), (10) for drugs for prevention and treatment of, for example, hypertrophic cardiomyopathy, arteriosclerosis, valvulopathy, myocardiac infarction (especially, myocardiac infarction post percutaneous transluminal coronary arterioplasty) and reangioplasty, (11) for drugs for treatment of hemorrhage of esophageal varicosis, cirrhosis and peripheral blood vessel disorders, (12) for drugs for treatment of, for example, diseases associated with general or local inflammation, for example, polyarteritis, rheumatoid arthritis, psoriasis, sunburn, eczema and allergy (for example, asthma, atopic dermatitis and allergic rhinitis) because they inhibit or modulate the secretion of physiologically active substances acting on the immune system (for example, Substance P, tachykinin and cytokines), (13) for drugs for treatment of, for example, dementia (for example, Alzheimer disease, Alzheimer-type senile dementia, vascular/multi-infarct dementia), headache, migraine, schizophrenia, epilepsy, depression, generalized anxiety disorder, sleep disorder, and multiple sclerosis, because they give influence on the production and secretion of nerve regulators, (14) for analgesic drugs, (15) for drugs for treatment of, for example, acute bacterial meningitis, acute virus encephalitis, adult respiratory distress syndrome (ARDS), bacterial pneumonia, severe systemic mycotic infection, tuberculosis, spinal damage, bone fracture, hepatic failure, pneumonia, alcoholic hepatitis, virus A hepatitis, virus B hepatitis, virus C hepatitis, AIDS infection, human papilloma virus infection, influenza infection, metastasis of cancer, multiple myeloma, osteomalacia, osteoporosis, bone Paget disease, reflux esophagitis, nephritis, renal failure, sepsis, septic shock, hypercalcemia, hypercholesterolemia, hypertriglyceridemia, hyperlipemia, systemic lupus erythematosus, transient ischemic attach and alcoholic hepatitis, (16) for cure of, for example, organ trasplant, burns, trauma, and alopecia, (17) ocular diseases for example glaucoma, (18) for imaging of tumors having somatostain receptor after introducing a radioactive substance (for example, .sup.123 I, .sup.125 I, .sup.111 In) to the compounds of the present invention either directly or via a proper spacer, and (19) targeting tumors with somatostatin receptors using the compounds in the present invention conjugated with anti-cancer drugs directly or using an appropriate spacer.

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                 Enhanced polymer searching in REGISTRY
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     ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS
L4
     Hibernating myocardium is characterized by viable myocardium with impaired
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     function due to localized reduced perfusion. Hibernating myocytes retain
     cellular integrity, but cannot sustain high-energy requirements of
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     norepinephrine, are believed to be predictive of mortality from
     hibernating myocardium. Likewise, high levels of catecholamines lead to
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     reduces plasma norepinephrine levels, and it thus is useful in a method of
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     136:350560 CA
     Treatment of hibernating myocardium and diabetic cardiomyopathy
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     with a GLP-1 peptide
     Ehlers, Mario
TN
     Coolidge, Thomas R., USA
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L1
           4598 S (GLP-1) OR (GLUCAGON-LIKE PEPTIDE-1)
L2
              1 S L1 (P) L2
L3
L4
              1 S L1 AND L2
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L6
       572641 SILICA?
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=> s polyethylene glycol?
       108169 POLYETHYLENE GLYCOL?
=> s 18 and 17 and 16 and 15
            1 L8 AND L7 AND L6 AND L5
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    ANSWER 1 OF 1 CA COPYRIGHT 2002 ACS
    A pharmaceutical or veterinary paste formulation comprises a drug, fumed
     silica, a viscosity modifier, a hydrophilic carrier, optionally,
     an absorbent and a dye, stabilizer, surfactant, or preservative.
                                                                      This
     invention also provides for methods of using these formulations for
     treating various disease states as well. Thus, a paste was prepared containing
     3-(cyclopropylmethoxy)-5,5-dimethyl-4-((4-methylsulfonyl)phenyl)-5H-furan-
     2-one (COX-2 inhibitor) 0.82, TiO2 0.2,
    MqCO3 2, fumed silica 4.25, and PEG-300 0.4% and
     triacetin qs.
     135:200445 CA
ΑN
TI
    Pharmaceutical or veterinary paste formulations containing silica
    and viscosity modifier
    Jun, Chen
IN
    Merial Limited, UK
PA
    PCT Int. Appl., 64 pp.
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    CODEN: PIXXD2
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    Patent
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    English
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L1 57011 S CARDIOMYOPATH?

L2 4598 S (GLP-1) OR (GLUCAGON-LIKE PEPTIDE-1)

L3 1 S L1 (P) L2 L4 1 S L1 AND L2

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<u>L8</u> 16 and 11	10	<u>L8</u>
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<u>L2</u> GLP-1	489	<u>L2</u>
<u>L1</u> cardiomyopath\$6	2716	<u>L1</u>

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57011 S CARDIOMYOPATH?

L2 4598 S (GLP-1) OR (GLUCAGON-LIKE PEPTIDE-1)

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L1